(2)

ANNUAL PROGRESS REPORT

Grant#: N00014-90-J-1697

PRINCIPAL INVESTIGATOR: Dr. Stephen J. Benkovic

INSTITUTION: The Pennsylvania State University

GRANT TITLE: Catalytic Antibodies

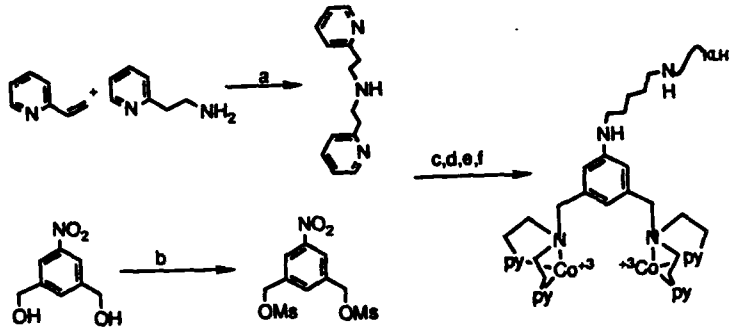
REPORTING PERIOD: March 15, 1992 - March 14, 1992

AWARD PERIOD: March 15, 1990 - March 14, 1993

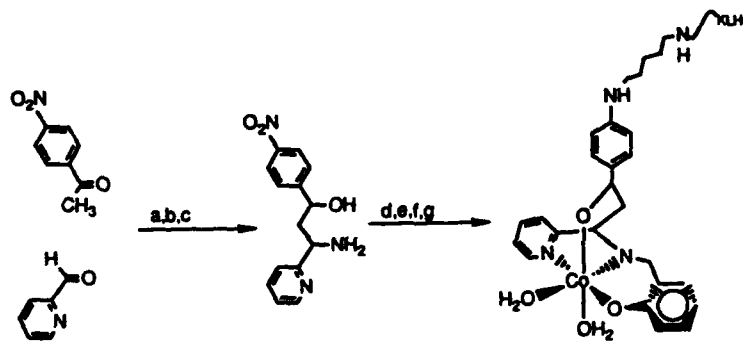
OBJECTIVE/APPROACH: To induce catalytic antibodies that promote redox reactions through the use of haptens that feature: 1) a nicotinamide cofactor and 2) a mono- or binuclear copper complex.

ACCOMPLISHMENTS (last 12 months): A3,4-disubstituted pyridine was synthesized (last Progress Report), conjugated to a carrier protein, and 20-monoclonal antibodies were isolated. These were tested for their ability to catalyze either a formate dehydrogenese reaction or the addition of cyanide anion to the pyridinium ring. No catalysis was found. Fluorescence titrations of the antibodies with the nicotinamide hapten both in the oxidized and reduced forms demonstrated binding affinities $>10^7$ M^{-1} for both oxidation states. We concluded that this set of antibodies was not recognizing the heterocylic portion of the hapten, therefore we discontinued studying them.

In parallel we synthesized the following two Co^{+3} haptens as models for mono- and binuclear copper complexes:

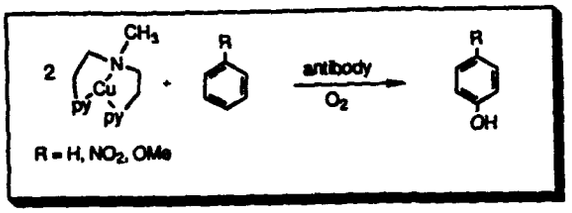


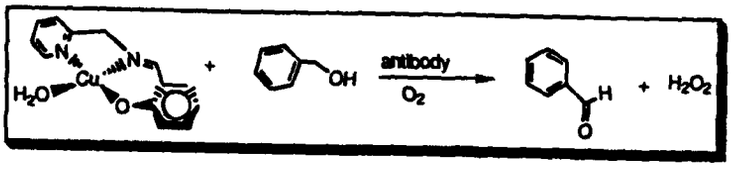
a.AcOH; b.MsCl, Et_3N; c.DIPEA; d.H_2, Pt; e.$CoCl_2$, HCl, O_2; f.KLH, glutaraldehyde, $NaBH_4$



a.NaOH; b.NH_4OH; c.$NaBH_4$; d.salicylaldehyde; e.H_2, Pt; f.$CoCl_2$; g. KLH, glutaraldehyde, $NaBH_4$

The resultant antibodies will be used to catalyze the following oxidations:





SIGNIFICANCE: Yet to be realized.

WORK PLAN (next 12 months): The specific objectives of the next year's work plan is to test the antibodies induced by haptens (1) and (2).

ANNUAL REPORT QUESTIONNAIRE
(for ONR use only)

Principal Investigator Name: Stephen J. Benkovic

Institution: The Pennsylvania State University

Project Title: Catalytic Antibodies

Number of ONR supported

Papers published in refereed journals: -0-

Papers or reports in non-refereed publications: -0-

Books or book chapters published: -0-

Number of ONR supported patents/inventions
Filed: -0-

Granted: -0- **Patent name and number:** -0-

Number of presentations: Total ONR Project

Invited: -0-

Contributed: -0-

Trainee Data (only for those receiving full or partial ONR support):

	TOTAL	FEMALE	MINORITY	NON-US CITIZEN
No. Grad. Students:				
No. Postdoctorals:	1	0	0	0
No. Undergraduates:				

AWARDS/HONORS TO PI AND/OR TO MEMBERS OF PI'S RESEARCH GROUP (please describe):

See attached CV

Equipment purchased on grant (number and description of items costing >$1,500):

N/A